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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/053,349	01/15/2002	Brian Lentricchia	11.019011	9843

38732 7590 12/21/2004

CYTYC CORPORATION
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MARLBOROUGH, MA 01752

EXAMINER

RILEY, JEZIA

ART UNIT	PAPER NUMBER
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1637

DATE MAILED: 12/21/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/053,349

Applicant(s)

LENTRICHIA ET AL.

Examiner

Jezia Riley

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 April 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-40 is/are pending in the application.
- 4a) Of the above claim(s) 1-15 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 16-28,30,31 and 36-40 is/are rejected.
- 7) ☒ Claim(s) 29 and 32-35 is/are objected to.
- 8) ☒ Claim(s) 1-40 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>8/8/03; 2/24/03; 11/27/02</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

1. Applicant's election of group II (claims 16-40) in the reply filed on 4/19/2004 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

3. Claims 16-20, 30, 31, and 36 are rejected under 35 U.S.C. 102(b) as being anticipated by Gevaudant et al. (Journal of Trace and Microphore Techniques, No. 1999, PP 445-450, abstract only).

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Gevaudant discloses an efficient method for isolation of total RNA, by combining polyvinylpyrrolidone and 2-butoxyethanol. The isolated RNA was suitable for hybridization and PCR.

4. Claims 16, 17, 22, 23-25, 37-40 are rejected under 35 U.S.C. 102(b) as being anticipated by Van Ness US 5,124,444.

The reference relates to compositions and assay methods for the extraction and hybridization of nucleic acids. In particular this invention relates to compositions and methods to extract nucleic acids from cells in complex biological samples or specimens.

The reference shows an alternative effective approach to using lactams in extracting total nucleic acid from complex biological samples, which surprisingly may be accomplished without heat is the use of certain competitive agents from the group consisting of alcohol, polysaccharide sulfate, and polymeric sulfonic acid in conjunction with guanidine salt lysing agents. After solubilizing the complex biological sample with a solution comprising the guanidine salt, the competitive agent is added at a molarity approximately comparable to or in excess of the guanidine salt. The extraction solution is made biphasic by the addition of an organic solvent such as lactam, phenol or chloroform and nucleic acid is isolated from the aqueous phase. No heat needs to be used in this extraction process. This process is particularly beneficial when GnSCN is used as the lysing agent. The competitive agent alcohols are selected from the group consisting of monohydroxyalkanes, dihydroxyalkanes, trihydroxyalkanes with a

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total carbon number not exceeding 20, monosaccharides, oligosaccharides, polysaccharides, monohydroxycycloalkanes, dihydroxycycloalkanes, trihydroxycycloalkanes and polyhydroxycycloalkanes. Preferably the alcohol will be a dihydroxyalkane, most preferably ethylene glycol. (col. 8, col 17).

The extraction and hybridization methods of the present invention may be applied to a complex biological mixture of nucleic acid (RNA and/or DNA) and non-nucleic acid. Such a complex biological mixture includes a wide range of eucaryotic and procaryotic cells, including protoplasts; or other biological materials which may harbor nucleic acids. The methods are thus applicable to tissue culture animal cells, animal tissue (e.g., heart, liver or brain, homogenized in lysis buffer), blood cells, reticulocytes, lymphocytes, plant cells or other cells sensitive to osmotic shock and cells of bacteria, yeasts, viruses, mycoplasmas, protozoa, rickettsia, fungi and other small microbial cells and the like. (col. 3-4, bridging paragraph)

5. Claims 16-28, 30, 31, 36-40 are rejected under 35 U.S.C. 102(e) as being anticipated by Lai et al. (US 6,503,716 B1).

Lai et al. discloses simple, fast and efficient methods for isolating nucleic acids from samples, typically from biological samples. Nucleic acid extraction reagents useful in the methods are typically aqueous compositions comprising sodium metasilicate and a substituted ether. Typical substituted ethers include, but are not limited to, alkoxy alkyl alcohols, aryloxy alkyl alcohols and alkyloxy aryl alcohols comprising from 2 to 12 carbon atoms, more typically from 3 or 4 to

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8 carbon atoms. Preferred substituted ethers are unbranched primary alkoxy alkanols. Examples of preferred alkylated alkyl alcohols include 2-butoxyethanol and 2-methoxyethanol.

The nucleic acid extraction reagents are typically basic, preferably having a pH in the range of about pH 7 to about pH 10, and may contain additional optional components, including but not limited to buffering agents such as Tris-HCl. The intended use of the extracted nucleic acid can influence the concentration of each of the ingredients used in the extraction reagent. For example, when the extracted nucleic acid will be used in a PCR reaction, the extraction reagent should be formulated such that the concentration of ingredients in the PCR reaction will not inhibit Taq polymerase or otherwise prevent the amplification reaction from working. (col.2-3) The nucleic acid extraction reagents and methods of the invention provide significant advantages over currently available isolation techniques. Quite importantly, nucleic acids isolated with the reagents and/or methods of the invention are substantially pure, and can be used directly in a variety of assays and/or analyses without further manipulation or purification. For example, nucleic acids isolated with the reagents and/or methods of the invention may be amplified, e.g. by PCR, or sequenced without further purification. The ability to efficiently isolate nucleic acids from a biological sample in a single step in high purity, especially in high enough purity for subsequent enzymatic manipulations such as PCR amplification, is unprecedented in the art. A significant advantage of the method of the invention is that the isolated nucleic acids may be used directly in further assays and experiments without further

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purification. For example, as demonstrated in Example 2, the recovered supernatant may be run directly on an agarose gel for direct analysis of the isolated nucleic acids. As demonstrated in Examples 2-13, DNA from a variety of different samples, including foodstuffs and blood, isolated according to the method of the invention was used directly in PCR amplification experiments.

According to those examples, the supernatant fraction was used directly as a source of template DNA for the PCR reaction. The supernatant fraction could also be used as a source of template DNA or RNA for other applications, such as sequencing, labeling reactions, or generating cDNA. (col.5 and see col. 9).

It has been observed that sometimes a flocculent becomes suspended in the nucleic acid extraction reagent, either during preparation or subsequent storage.

Once formed, the flocculent may be redissolved by gentle agitation and/or application of heat. (col.8, lines 34-38). Thus, the temperature used should not be so high as to denature or otherwise degrade the nucleic acids to be extracted. Typically, temperatures ranging from ambient (approx. 25.degree. C.) to about 120.degree. C., more typically from about 55.degree. C. to about 100.degree. C. yield good results. (col. 8, lines 60-65).

The source of the nucleic acid can be any cell or virus, or any other composition, housing or structure comprising a nucleic acid. The sample can contain any substance derived from an animal subject, for example, blood, cerebral spinal fluid, hair, fur, saliva, sputum, semen, urine, stool, mucous, skin, a benign or malignant tumor or growth, biopsied tissue or any other type of tissue sample used in diagnosing a disease or condition. The subject can be any kind of animal,

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for example, a human. Alternatively, the sample can contain any substance derived from a plant subject, for example, leaf, stem, stalk, pollen, root, branch, flower, seed, bulb, spore or other plant material. (col. 10-11).

Example 1 describes preparation and composition for extracting nucleic acid.

Said preparation lacks a chloroform extraction step, a phenol extraction, phenol/chloroform extraction, or an alcohol precipitation.

6. Claims 29, 32-35 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Information Disclosure Statement

7. The information disclosure statement filed 11/27/02 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered and lined through.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jezia Riley whose telephone number is 571-272-0786. The examiner can normally be reached on 9:30AM - 5:00PM.


If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax

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phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Wednesday, December 15, 2004



JEZIA RILEY
PRIMARY EXAMINER